

## Clonal precursor of bone, cartilage, and hematopoietic niche stromal cells.

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### Public Summary:

Organs are composites of tissue types with diverse developmental origins, and they rely on distinct stem and progenitor cells to meet physiological demands for cellular production and homeostasis. How diverse stem cell activity is coordinated within organs is not well understood. Here we describe a lineage-restricted, self-renewing common skeletal progenitor (bone, cartilage, stromal progenitor; BCSP) isolated from limb bones and bone marrow tissue of fetal, neonatal, and adult mice. The BCSP clonally produces chondrocytes (cartilage-forming) and osteogenic (bone-forming) cells and at least three subsets of stromal cells that exhibit differential expression of cell surface markers, including CD105 (or endoglin), Thy1 [or CD90 (cluster of differentiation 90)], and 6C3 [ENPEP glutamyl aminopeptidase (aminopeptidase A)]. These three stromal subsets exhibit differential capacities to support hematopoietic (blood-forming) stem and progenitor cells. Although the 6C3-expressing subset demonstrates functional stem cell niche activity by maintaining primitive hematopoietic stem cell (HSC) renewal in vitro, the other stromal populations promote HSC differentiation to more committed lines of hematopoiesis, such as the B-cell lineage. Gene expression analysis and microscopic studies further reveal a microenvironment in which CD105-, Thy1-, and 6C3-expressing marrow stroma collaborate to provide cytokine signaling to HSCs and more committed hematopoietic progenitors. As a result, within the context of bone as a blood-forming organ, the BCSP plays a critical role in supporting hematopoiesis through its generation of diverse osteogenic and hematopoietic-promoting stroma, including HSC supportive 6C3(+) niche cells.

### Scientific Abstract:

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